MEDINFO 2019: Health and Wellbeing e-Networks for All
L. Ohno-Machado and B. Séroussi (Eds.)

doi:10.3233/SHTI190191

An Interactive Timeline Visualization for Patient Cohorts in the Oncological Routine: A Use Case on Multiple Myeloma

Julia Dieter[a], Janko Ahlbrandt[a], Alexander Knurr[a], Janine Al-Hmad[a] and Frank Ückert[a]

[a] *Division of Medical Informatics for Translational Oncology, German Cancer Research Center (DKFZ), Heidelberg, Baden-Württemberg, Germany*

Abstract

With the growing interdisciplinarity of cancer treatment and increasing amounts of data and patients, it is getting increasingly difficult for physicians to capture a patient's medical history as a basis for adequate treatment and to compare different medical histories of similar patients to each other. Furthermore, in order to tackle the etiological mechanisms of cancer, it is crucial to identify patients exhibiting a different disease course than their corresponding cohort. Several timeline visualizations have already been proposed. However, the functions and design of such visualizations are always use case dependent. We constructed a cohort timeline prototype mock-up for a specific oncological use case involving multiple myeloma, where the chronological monitoring of various parameters is crucial for patient diagnosis and treatment. Our proposed cohort timeline is a synthesis between elements described in the literature and our own approaches regarding function and design.

Keywords:

Clinical Decision-Making, Cohort Studies, Data Mining

Introduction

For the treatment of cancer, physicians need to consider comprehensive information about the patients, including the medical history [1] as well as current events such as examination results. The information mainly comprises basic variables such as age, gender, education, and clinical variables such as details on diagnoses, therapies, staging results, laboratory analyses, and further examinations. However, those variables are usually stored in different systems within the hospital, e.g., the laboratory information system or the hospital information system. The data then have to be chronologically realigned in a manual fashion by physicians, often under time pressure. Thus, there is a great need for tools creating a chronological overview of patient data, helping to save time, and preventing errors.

To support physicians in the compaction and comparison of salient patient information as well as in the chronological realignment of data from different sources, several approaches have been developed for integration and visualization of medical patient histories. There are tools for either single patient (e.g., LifeLines, KNAVE-II; [2–4]) or for patient cohorts (e.g., LifeLines2, VISITORS; [4–7]), and they aim to display various data types, such as numerical data (e.g., MIVA), categorical data or both (e.g., WBIVS; [4,8]).

A fundamental work for the display of a single patient medical history is the LifeLines approach of Plaisant et al. [2]. It is not restricted to oncology and aims at displaying the key information of a single patient's medical history by aligning zoomable lanes on top of each other. Depending on the task at hand, they can be opened up or closed [2,4]. It focuses on categorical data. The lanes represent different areas of the patient record such as "Problems", "Diagnoses" or "Tests", while single events are encoded within the lanes. For instance, the lane entitled "Tests" harbors examination events such as "Blood" or "ECG" etc. The separate markings within the lane are positioned according to their corresponding chronological position on the x-axis, which is located at the bottom of all lanes. Design aspects such as line thickness reflect the severity of medical problems. Detailed information on an event is given in a separate window, which can be summoned by clicking on the respective event in the main view. Further interactive features include a mouseover function (i.e., displaying information when hitting a label with the cursor), zooming, alerts and a search option for keywords such as symptoms (e.g., "migraine"). KNAVE-II is another visualization architecture for time-oriented clinical patient data and has been implemented and tested in the oncological domain [3]. Similar to Lifelines, it comprises horizontally stacked views, but in contrast to the former, KNAVE-II offers domain-specific groupings as well as temporal abstractions to enable interactive data manipulation and exploration [3,9]. However, drawbacks of Lifelines and KNAVE-II might be crowding problems, i.e., the display might become too complex due to increasing timespans and number of events [2].

Approaches to the chronological display of patient cohorts have also been developed. Bernard et al. [10] developed a network of static dashboards to visualize the medical histories of a post-operative prostate cancer cohort. Each separate dashboard represents a temporal segment of the cohort, i.e., one part of time-ordered temporal data. Each dashboard is composed of different visualizations such as bar charts, pie charts or box plots. The chronological connection, i.e., the medical history of the cohort, is represented by the network that is constructed based on the connections between the single dashboards. Unfortunately, the tool has not been validated as previous visualization approaches. Thus, its efficiency in the real world setting still remains uncertain. The tool does not support the traditional timeline display, so that physicians might need extended training. In addition, the data processing steps underlying the temporal segmentation of data might be hard to follow and only a limited number of EHR elements might be shown within the dashboard due to space issues.

The LifeLines2 approach uses a classical timeline visualization, just like its predecessor LifeLines. It enables the display of temporal categorical data for multiple patient records. The lanes are stacked vertically and represent each single cases, with event markers color-coded on the corresponding positions at the horizontal time axis [11]. All records can be aligned by a specific event in chronological display [4]. The alignment can also be achieved according to a specific events, e.g., the second diagnosis. Furthermore, users are able to filter and search for specific event sequences; and the temporal distribution of selected event types can be displayed by histogram [4,11]. In addition, approaches such as Similian, which extended LifeLines2 with a similary measure, enable the search for similar medical patient histories [4,12]. However, LifeLines2 displays one patient record per horizontal lane, so that not all records can be viewed simultaneously in larger patient cohorts due to space issues [13]. In addition, numerical data have to be preprocessed as the approach focuses on categorical data only.

The VISITORS system by Klimov et al. [7], an extension of KNAVE-II, is a visualization and exploration tool for time-oriented, categorical as well as numerical data of multiple patients. VISITORS is also constructed of horizontal lanes that are associated with a horizontal, chronological x-axis and enables the display of raw data as well as abstracted concepts for overviews. However, the tool does not enable the display of multiple numerical parameters within one lane. When several lanes for different numerical parameters need to be applied, not all lanes might be viewed within one window.

Taken together, there exist various cohort timeline visualizations for different application scenarios and data types, also exhibiting multiple interactive features. Yet, as the literature about the cohort timelines shows, their configuration and functionalities mostly depend on a specific use case for which they are constructed or adapted. Thus, there does not exist one universal solution for all use cases.

The visualizations in clinical routine is still in high demand, as no approaches are widely deplayed yet [14]. As such, we developed a timeline for cohort in clinical oncological routine, adapted to the specific use case of multiple myeloma (MM; ICD10: C90.0) within the first-line therapeutic setting. It could become apparent for the need to monitor several parameters over time and to compare the course of one patient to a corresponding cohort by applying such tool (see below).

MM can arise from two pre-stages, i.e., the Monoclonal Gammopathy of Undetermined Significance (MGUS) or the smoldering myeloma [15]. Both conditions are lacking in treatment indication and can be differentiated from the MM and monitored by several parameters such as clonal plasma cells in the bone marrow, monoclonal protein in the serum and urine as well as end organ damage [15]. The transition from the pre-stages to an MM is marked by the fulfillment of one or more of the SLiM-CRAB criteria (an acronym standing for ">60% clonal plasma cell content in the bone marrow", "free light chain ratio in the serum >100", ">1 focal lesion >1cm in MRI imaging", "Calcium", "renal insufficiency", "anemia" and "bone lesions"; [16,17]). Those criteria comprise several laboratory parameters (e.g., calcium, creatinine and hemoglobin), bone lesions as determined by imaging, the percentage of clonal plasma cells in the bone marrow, the free light chain ratio in the serum and focal lesions as determined by MRI [15].

In addition, although the steps for treatment are given in the MM treatment guideline, it might still be necessary to decide between different treatment options. Those decisions have to be made individually, for instance, the decision in favor of or against an autologous stem cell transplantation. Especially in the cases of older patients, it becomes increasingly important to weight the burden of therapeutic side effects against the potential treatment benefit. To support decision making, it might be of help to compare one patient's medical information with treatment profiles from previous patients and their treatment outcomes.

We therefore developed the MM use case-specific prototype mock-up of an interactive cohort timeline.

Methods

The construction of our cohort timeline was based on a combination of timeline functionalities and design aspects collected from a literature review and our own approaches to these issues.

The prototype mock-up of the proposed cohort timeline was developed in iterative cycles with clinical, medical informatics as well as biological inputs. We adapted the concept of horizontal lanes from previous tools, such as LifeLines, LifeLines2 and VISITORS, for visualizing the medical history of patients [2–4,7,9]. Functionalities for interactive data visualization were designed and incorporated to meet physician's needs and suggestions of previous studies [4–7,11].

The parameters in our prototype mock-up were selected based on the MM treatment guideline for diagnosis, therapy and the monitoring of the remission status, including the laboratory values, the designations of therapy steps as well as the criteria for evaluating the treatment response. In addition, the International Myeloma Working Group (IMWG) and the revised-Myeloma Comorbidity Index (R-MCI) were also included, which have been suggested to be useful in identifying geriatric risk profiles and prognostic values for functional decline among older multiple myeloma patients [18]. They are calculated by a combination of weights among various parameters including age, comorbidities and the ability to perform activities of daily living (e.g., self-care and household) [19]. Therefore, those scores are referenced as relevant decision criteria to differentiate between treatment options documented in the MM treatment guideline, especially for older patients.

We documented our general design and planned interactive funcions in a detailed prototype mock-up by a user experience specialist.

Results

The proposed interactive cohort timeline is built up of vertically stacked lanes, each comprising one key clinical component such as information on the general patient condition (IMWG score, R-MCI), laboratory data, treatment options and information on the treatment response, which are all significant for diagnosing, treating or monitoring MM. This sequence of events during patient treatment is reflected in the vertical order of the lanes from top to bottom (see Figure 1).

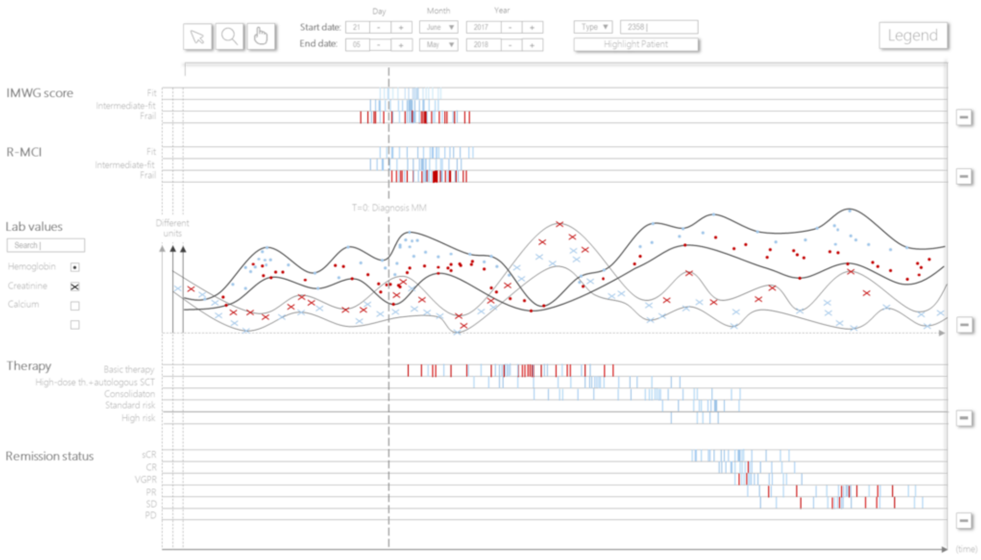

Figure 1: Prototype mock-up of the use case-specific cohort timeline

Each lane depicts all corresponding data points of the selected cohort. In case of visualizing multiple cohorts, the latter are color-coded in order to be distinguished within the same lane. The associations of laboratory values to their parameters are represented by data points, e.g., dots and crosses (see Figure 2).

The chronological reference of the visualization is given by a time-harboring x-axis at the bottom of all lanes. The vertically stacked lanes can be chronologically compared and referenced to the horizontal time axis by means of a thin vertical marker that spans all lanes (similar to the Data Point Scrubber of Faiola et al. [20]) and follows the cursor.

The visualization type for each lane is content-specific. Laboratory values are presented in an x-y-diagram-lane. Different laboratory parameters are visualized within the same lane. Upper and lower flanking lines that connect the lowest and highest values, respectively, indicating the value range. A filtering option next to the lane allows the selection of single laboratory parameters or functional parameter sets.

The occurrence of events such as treatments or evaluation of a remission status is marked in the corresponding lane by a small vertical line per patient at the corresponding time point (i.e., position on the time axis).

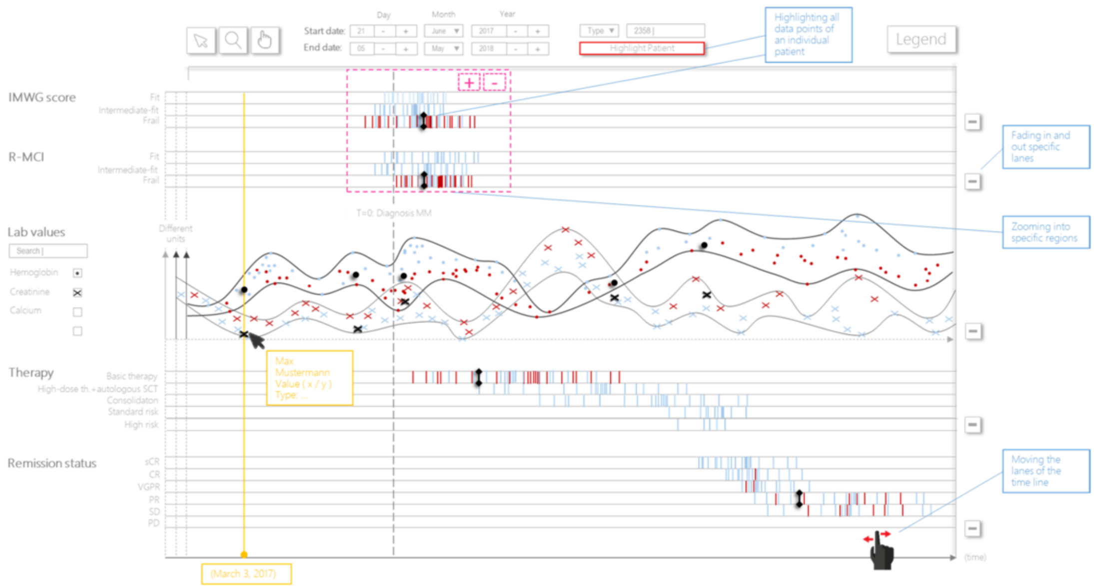

Figure 2: Proposed interactive features for the cohort timeline

Given a specific use case, a user might want to read the values in an absolute timeline or a relative one to a defined reference time point. For instance, the time of diagnosis of a specific disease might serve as reference, relative to all other events that are calculated and displayed chronologically for each individual patient. Therefore, similar to VISITORS [7], an option to choose between absolute and relative chronological display will be integrated. The options to switch between different parameters of reference [4–6] as well as the selection of a time window of interest will also be given [4,7].

Additionally, lanes can be faded in and out depending on the use case at hand [2]. Further interactive features include a hover over function (similar to Wang et al. [11]), displaying the patient-ID as well as the corresponding value when hitting a data point with the cursor. In addition, all data points from a specific patient shall be highlighted throughout the cohort timeline in order to enable the comparison to a corresponding cohort. To differentiate compact or clustered data, a zoom function will be included (e.g., [2]). In the case where a lane is too cluttered with data points or if subcohorts are to be selected, a filtering function is also added. This is enabled by checking or unchecking selection boxes on a target lane or simply by marking specific data points. In case of visualizing long time spans, a sideward scroll is included as well as an option to constrain the time window for which data are to be displayed. A retractable legend is included. Furthermore, certain users such as physicians in different specialities might have different preference on the ways to display the cohort information in timeline. And customized configurations can be saved for future use to save time. An export function for data and images will also be provided. An example of the general cohort timeline design is shown in Figure 1. The interactive functionalities are presented in Figure 2.

Discussion

The literature shows a multitude of approaches for temporal visualizations for medical histories of patient cohorts, including a variety of interactive features. However, it is also obvious that each timeline has to be adapted to a specific use case in order to see if the approach can address the specific questions in different user scenarios.

We developed a prototype mock-up for the oncological use case of diagnosing, treating and monitoring MM, as a synthesis between designs and functionalities of previous cohort timelines and our own ideas.

As described above, a physician might want to weight the burden of therapeutic side effects against the potential treatment benefit for an old MM patient. In this case, the physician plots two cohorts of previous MM patients onto the timeline: One having received stem cell transplantation as well as high-dose therapy (blue cohort in Figure 1 and Figure 2, appearing brighter in the black and white view) and another one having received basic therapy only (red cohort, appearing darker in the black and white view). Patients categorized as "frail" in the IMWG score and the R-MCI have higher creatinine and lower hemoglobin levels after therapy than fitter patients and a less optimal treatment response (e.g., remission status=stable disease).

The data points of a current patient can now be plotted, highligted and compared to the two cohorts to estimate potential treatment outcomes with and without SCT and high-dose therapy. The example patient might rather resemble the cohort not suited for SCT and high-dose therapy in our prototype mock-ups.

In a future step, the prototype mock-up presented here shall serve as a basis for an evaluation by end users. Although the prototype mock-up was constructed based on realistic data and procedures as much as possible, it has to be taken into account that the plot has not been programmed and tested with real data yet. Thus, the behavior of the plot in real live scenarios presently cannot be anticipated.

Conclusions

We present a compact, interactive cohort timeline visualization approach to display multidimensional data points of oncological cohorts in a chronological reference frame. Our prototype mock-up shall serve as a basis for a comprehensive evaluation by physicians as potential end users. Although our visualization has not been realized and tested with real data yet, it might become a promising tool for physicians to support decisions in treatment of oncological patients, hypothesis generation, and the exploration of the etiological mechanisms underlying cancer.

Acknowledgements

This work was conducted within the frame of the DataThereHouse (DTH) project in cooperation with the National Center for Tumor Diseases (NCT) Heidelberg, supported by the Federal Ministry of Education and Research (BMBF). The project is concerned with the integration of data from different sources including the Heidelberg University Hospital as well as the German Cancer Research Center (DKFZ) Heidelberg for all oncological entities.

References

[1] Drohan B, Grinstein G, Hughes K (2010) Oncology Lifeline - A Timeline Tool for the Interdisciplinary Management of Breast Cancer Patients in a Surgical Clinic. In *2010 14th International Conference Information Visualisation,* Staff I, ed. I E E E, [Place of publication not identified], pp. 233–238.

[2] Plaisant C, Mushlin R, Snyder A, Li J, Heller D, Shneiderman B (1998) LifeLines: Using visualization to enhance navigation and analysis of patient records. Proc AMIA Symp, 76–80.

[3] Shahar Y, Goren-Bar D, Boaz D, Tahan G (2006) Distributed, intelligent, interactive visualization and exploration of time-oriented clinical data and their abstractions. Artif Intell Med 38, 115–135.

[4] Rind A, Wang TD, Aigner W, Miksch S, Plaisant C, Wongsuphasawat K, Shneiderman B (2013) *Interactive Information Visualization to Explore and Query Electronic Health Records,* Now Publishers.

[5] Wang TD, Plaisant C, Quinn AJ, Stanchak R, Murphy S, Shneiderman B (2008) Aligning temporal data by sentinel events. In *The 26th Annual CHI Conference on Human Factors in Computing Systems, CHI 2008: Conference proceedings ; April 5-10, 2008 in Florence, Italy,* Burnett M, ed. ACM, New York, NY, p. 457.

[6] Wang TD, Plaisant C, Shneiderman B, Spring N, Roseman D, Marchand G, Mukherjee V, Smith M (2009) Temporal summaries: supporting temporal

categorical searching, aggregation and comparison. IEEE Trans Vis Comput Graph 15, 1049–1056.

[7] Klimov D, Shahar Y, Taieb-Maimon M (2010) Intelligent visualization and exploration of time-oriented data of multiple patients. Artif Intell Med 49, 11–31.

[8] Stevens SS (1946) On the Theory of Scales of Measurement. Science 103, 677–680.

[9] Ordóñez P, desJardins M, Lombardi M, Lehmann CU, Fackler J (2011) An animated multivariate visualization for physiological and clinical data in the ICU. In *Ihi 10 Proceedings of the 2010 Acm International Health Informatics,* Committee I'1C, ed. Association for Computing Machinery, New York, p. 771.

[10] Bernard J, Sessler D, Kohlhammer J, Ruddle RA (2018) Using Dashboard Networks to Visualize Multiple Patient Histories: A Design Study on Post-operative Prostate Cancer. IEEE Trans Vis Comput Graph.

[11] Wang TD, Wongsuphasawat K, Plaisant C, Shneiderman B (2011) Extracting Insights from Electronic Health Records: Case Studies, a Visual Analytics Process Model, and Design Recommendations. J Med Syst 35, 1135–1152.

[12] Wongsuphasawat K, Shneiderman B (2009) Finding comparable temporal categorical records: A similarity measure with an interactive visualization. In *IEEE Symposium on Visual Analytics Science and Technology, 2009, VAST 2009: 12-13 Oct. 2009, Atlantic City, New Jersey, USA ; proceedings,* Stasko J, ed. IEEE, Piscataway, NJ, pp. 27–34.

[13] Guerra Gómez, John Alexis & Wongsuphasawat, Krist & David Wang, Taowei & Pack, Michael & Plaisant, Catherine & Wang, K. (2011) Analyzing Incident Management Event Sequences with Interactive Visualization.

[14] Wanderer JP, Nelson SE, Ehrenfeld JM, Monahan S, Park S (2016) Clinical Data Visualization: The Current State and Future Needs. J Med Syst 40, 275.

[15] Wörmann, B., Driessen, C., Einsele, H., Goldschmidt, H., Gunsilius, E., Kortüm, M., Kröger, N., Ludwig, H., Mügge, L.-O., Naumann, R., Pritzkuleit, R., Röllig, C., Scheid, C., Taverna, C., Weisel, K., Weißinger, F. (2018) *Multiples Myelom: Leitlinie*.

[16] Boquoi A, Strapatsas J, Fenk R, Haas R (2018) Multiples Myelom. Klinikarzt 47, 418–425.

[17] Willenbacher E, Balog A, Willenbacher W (2018) Short overview on the current standard of treatment in newly diagnosed multiple myeloma. memo - Magazine of European Medical Oncology 11, 59–64.

[18] Engelhardt M, Dold SM, Ihorst G, Zober A, Möller M, Reinhardt H, Hieke S, Schumacher M, Wäsch R (2016) Geriatric assessment in multiple myeloma patients: Validation of the International Myeloma Working Group (IMWG) score and comparison with other common comorbidity scores. Haematologica, haematol.2016.148189.

[19] Roehrig B, Hoeffken K, Pientka L, Wedding U (2007) How many and which items of activities of daily living (ADL) and instrumental activities of daily living (IADL) are necessary for screening. Critical Reviews in Oncology/Hematology 62, 164–171.

[20] Faiola A, Boston-Clay C, Jones J, Downey M, Newlon CM (2012) Managing Patient Health Across Diverse Spaces: Using Activity Theory to Model Pervasive Decision Support, https://scholarworks.iupui.edu/bitstream/1805/6153/1/Faiola_2012_managing.pdf.

Address for correspondence

Dr. Julia Dieter
Research Associate
Division of Medical Informatics for Translational Oncology

German Cancer Research Center (DKFZ)
Foundation under Puplic Law
Im Neuenheimer Feld 280
69120 Heidelberg
Germany
phone: +49 6221 42-5115
fax: +49 6221 42-5109

j.dieter@dkfz-heidelberg.de
https://www.dkfz.de/en/mitro/